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**EASTMAN**

**AR201-14083**

Eastman Chemical Company  
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November 14, 2002

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Ms. Christine Todd Whitman, Administrator  
U.S. EPA  
P.O. Box 1473  
Merrifield, VA 22116

ORIGINAL

Attn: Chemical Right-to-Know Program

**RE: HPV Chemical Challenge Program, AR-201**

Dear Ms. Whitman:

This letter is submitted by Eastman Chemical Company ("Eastman") in response to comments received from the Environmental Protection Agency ("EPA") dated November 8, 2002 following EPA's review of the test plan and robust summaries for 1,4-cyclohexanedimethanol (CHDM; CAS No.: 105-08-8). I would like to thank the EPA for its review and welcome the recognition of its completeness and fulfillment of Eastman's obligation to this chemical in the HPV program.

Below are the EPA's comments to our test plan and various robust summaries, and our responses:

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient).

1. "*Vapor pressure*. The submitter provided an estimated vapor pressure value of 0.000371 mm Hg (0.049 Pa) using MPBPWIN. Calculated values are acceptable only when the value is less than  $10^{-5}$  Pa at 25 °C (OECD). The submitter needs to provide measured data for this endpoint according to OECD guidelines."

A measured value was identified within Company files and a new summary has been prepared using that value.

2. "*Water solubility*. The submitter provided an estimated water solubility value which is much lower than a measured value EPA identified in the literature (Gerhartz, 1985). An explanation of this discrepancy is needed. [Gerhartz, W.(ed.) Ullmann's Encyclopedia of Industrial Chemistry. 5<sup>th</sup> ed. Volume A1. p. 312. Deerfield Beach, FL: VCH Publishers, 1985.]"

The information from this reference was obtained and a new summary has been prepared using that value.



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Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

1. "*Biodegradation*. The submitter tested the biodegradation of this substance using a Zahn-Wellens/EMPA test for inherent biodegradability that was done in accordance with OECD Guideline 302B. No biodegradation data were found in the literature by the Agency. Inherent biodegradability data can be considered adequate only if a substance does not degrade in such a test. Positive results in inherent tests indicate only that a substance is "not persistent," whereas negative results may be taken to mean that a substance is nonbiodegradable. Positive results are not sufficient to adequately characterize the behavior of the compound in the environment. The submitter needs to provide ready biodegradation data following OECD Guideline 301."

The data requirements for the HPV program on occasion differ from those of the OECD SIDS program. The following is an excerpt from the EPA guidelines dated 2/10/99 on the HPV website entitled "Determining the Adequacy of Existing Data": *Biodegradation (OECD Guidelines 301a-f for ready biodegradability, 302a-c for inherent biodegradability)*. Thus, I believe the data presented should be deemed acceptable for the purposes of the HPV program.

2. "*Transport and distribution (fugacity)*. The submitter needs to incorporate the actual input values utilized in its estimation of this endpoint."

The fugacity information was updated using the new vapor pressure and water solubility values.

Ecotoxicity (fish, invertebrates, and algae).

1. "Data are adequate for fish and algae. Although the submitter provided a daphnia study of 96-hours rather than a 48-hour study, the study, in this case, is considered adequate to address this endpoint for the purposes of the HPV Challenge Program."

Health Effects (acute toxicity, repeat dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

"Data are adequate for repeated-dose, developmental toxicity and the genetic toxicity endpoint of chromosomal aberrations. The data for acute toxicity was not adequate but, based on the weight of the evidence, no additional testing is needed for the purposes of the HPV Challenge Program. It appears that the reproductive endpoint was addressed adequately by the study conducted but an appropriate robust summary was not supplied. Data may be adequate for the genetic endpoint of gene mutations, however, enough detail has not been provided."

1. "*Acute toxicity*. The study was deficient, as described in the comments on robust summaries section, however, other information available indicates that the substance does not exhibit a high degree of acute toxicity and no further testing is needed. The purity of the test material was unknown. The age, sex, strain, and body weight of the rats were not given. It is unclear how many animals were tested (10 total or 10 per dose). It was unclear whether the rats were fasted prior to dosing, whether the decedent rat was in the highest dosing group, and if necropsy was performed. In addition, the LD<sub>50</sub> calculation method was not given."

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Unfortunately, due to the date (1965) at which this study was conducted, the requested details are not available for incorporation into the robust summary. The remarks section makes note to the fact that many details were not available.

2. "*Reproductive toxicity*. A reproductive and developmental toxicity screening test (OECD TG 421) was submitted. Although reproductive effects are mentioned in the robust summary for developmental effects, a separate robust summary is needed for the reproductive toxicity endpoint. Detailed information is needed for parameters showing effects. Even though effects were reported only at the highest dose level, detailed information concerning these parameters for all dose levels would be useful. Details are needed for the developmental parameters observed."

Since the study reported was an OECD 421 study and assessed both developmental and reproductive endpoints the results of both these parameters was presented in the one summary.

Detailed information was presented at the highest dose only as this is the only dose at which effects were noted. The robust summary states that effects were only seen at the highest dose so there is nothing to detail for any of the other dose levels. There were no developmental effects seen to detail and the NOAEL listed was the highest dose.

3. "*Genotoxicity (gene mutations)*. The Ames assay was not conducted at a high enough concentration. The maximum concentration used, 500 ug per plate, was one-tenth of the recommended concentration. However, if the substance was tested at this level because of cytotoxicity, then inclusion of information on the levels at which cytotoxicity occurred relevant to the dose selected would be sufficient to satisfy this endpoint. Otherwise, another test is needed. In addition to the cytotoxicity question identified above, other deficiencies noted were: only one plate was tested per concentration when three are recommended and there was no indication of which positive controls were used with which strains and whether the responses obtained were appropriate."

After reviewing the test report it was determined that the doses utilized were based on the presence of cytotoxicity and the robust summary has been modified to reflect this. In addition, detail has been added in regard to which positive control chemical was used for each strain. The above noted deficiencies as well as the period in which the study was conducted (i.e., pre-GLP) resulted in a reliability score of "Reliable with restrictions".

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Enclosed with this letter is a computer diskette containing the modified test plan and robust summaries in Adobe Acrobat (.pdf) format. The HPV registration number for Eastman Chemical Company is

Sincerely,

James A. Deyo, D.V.M., Ph.D., D.A.B.T.  
Senior Technical Associate

Enclosure